

RESEARCH ON PATHOGENESIS OF LYME BORRELIOSIS (LYME DISEASE)

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National Institute of Allergy and Infectious Diseases

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Date: June 1, 1989

Application Receipt Date: August 1, 1989

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institute of Allergy and Infectious Diseases (NIAID) announce the availability of an RFA for funding Research on Pathogenesis in Lyme Borreliosis (Lyme disease). This RFA (available upon request) invites applications for funding of research that will increase our understanding of interactions between *Borrelia burgdorferi* and the human host. Increased knowledge in this area will result in substantial improvements in diagnosis and chemotherapy and provide the basis for the development of an effective vaccine. Research projects involving use of tissue culture, animal models, human subjects, molecular techniques and other experimental approaches may be focused upon one or more of the following:

- o Identification and characterization of bacterial factors that act as virulence and colonization factors.
- o Identification and characterization of antigenic and immunogenic determinants presented to the host. The role of antigenic variation in pathogenicity. The mechanism of antigenic variation.
- o The nature of the immune response to *B. burgdorferi*? The relationships between the cell-mediated and humoral responses to *B. burgdorferi*. Characterization of host reactions; protective versus non-protective, specific

(to *B. burgdorferi*) versus non-specific. Classes of immunoglobulins produced in response to infection.

- o Characterization of the course of infection after *B. burgdorferi* enters the human host. Identification of organ systems and tissues that are infected and/or inflamed. Characterization of specific tissue tropisms.

- o Characterization of inflammatory responses in relation to the various clinical manifestations associated with Lyme borreliosis. The roles of cytokines in inflammatory responses in this disease.

- o Histopathologic studies of early and late manifestations of the disease.

- o The role of host immunogenetic determinants in susceptibility to the disease and its various manifestations.

- o Development of animal and/or tissue culture models that can be used to obtain insights or answers to the above questions.

- o Development of an improved culture medium that will allow maintenance of *B. burgdorferi* in a virulent form with greater maximum population density.

- o Development of a genetic transfer system in *B. burgdorferi*.

- o Comparison of pathogenesis of Lyme borreliosis with that of other spirochetal diseases such as syphilis and relapsing fever.

Applicants may include several of the above areas in their research proposals. Applicants are encouraged to consider other avenues of investigation that would be appropriate to the goals of this RFA as well.

Awards will be made as individual research project (R01) grants.

Domestic universities, medical colleges, hospitals, laboratories and other public or private research institutions, including State and local government units, are eligible to apply for funding. Awards under this announcement to foreign institutions will be made only for research of unusually high merit, need and

promise, and in accordance with Public Health Service policy governing such awards.

This is a one-time solicitation for proposals. Ten to 15 awards may be funded on the basis of merit and availability of funds.

The full RFA may be obtained from:

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